Detailed Response

I. Disposition of Claims

Claims 1, 6, 9-35, 37-41, 43, 69, 72-78, 83-87, 93-94 are pending. Claims 95 and 96 have been added. Claims are subject to an election of species such that any polymeric moiety recited as an outer membrane in instant claim 6 is viewed to meet the limitation of outer membrane polymer.

II. Rejections--35 USC §112, First Paragraph

The Examiner has rejected claims 1, 6, 9-35, 37-41, 43, 69, 72-78 (NOTE: the Official Action appears to have a typographical error {*sic.* "72-7"} but Applicants assume Examiner intended all of claims 72-78 to be rejected under this basis), 83-87, 93-94 under 35 U.S.C.112, first paragraph based upon the conclusion that there does not appear to be a written description of the claim limitation "wherein a polymer of the polymer outer membrane does not extend from the polymer outer membrane into the microcapsules such that two or more liquid phases are not dispersed by the polymer," in the application as filed. Applicants concur with the Examiner's opinion in this instance and apologize for any diversion the subject language has caused from the more important §102 and §103 issues, and has amended the claims containing that limitation (or similar language) to eliminate the limitation recited above. The Applicants respectfully request that this basis for rejection is removed from the case. In particular, claims 24-29 and newly added claims 95 and 96 are now free of any basis for rejection and allowance is requested.

III. Rejections--35 USC §102(b), Claims 1, 9, 11, 14, 17, 21-23, 30-35, 37-38, 40, 73-75, 85-86

Claims 1, 9, 11, 14, 17, 21-23, 30-35, 37-38, 40, 73-75, 85-86 stand rejected by the Examiner under 35 U.S.C. §102(b) as being anticipated by McGinity et al. US Patent 5,288,502,

hereinafter referred to as McGinity. A rejection under 35 U.S.C. §102 must contain every element recited in the claim in as complete detail as is contained in the claim and arranged as recited in the claim. MPEP §2131 provides:

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference. *Verdegall Bros. v. Union Oil Co. Of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim.

The Examiner states that since the pending claims are directed to composition of matter claims and not method claims, then Applicants' arguments relating to how McGinty's process leads to composition of matter differences (as compared to Applicant's composition of matter) has no merit. This statement is indeed curious because the Applicants are attempting to objectively explain how McGinty's microcapsules do not and cannot contain all of Applicants' claimed compositions (as amended) using deductive logic. Wherein this line of argument is directly related to rebutting the Examiner's inherency arguments. The Applicants respectfully request that the Examiner reconsider this issue and the Applicants will earnestly attempt to argue their points clearer and with greater focus in this paper.

Relative to the §102 rejection, the Applicants respectfully disagree as to the claims *as amended*. The Applicants respectfully argue that because from the facts derived from the reference, as set forth below, the cited reference does not contain every element recited in the rejected claims in as complete detail as is contained in the claims and arranged as recited in the claims. Thus, the rejection is unsupported by the art and should be withdrawn for the following reasons.

III.A. Flexible vs. Hardened

First, all independent claims have been amended to include the structural characteristic of a flexible polymer outer shell. Support for this amendment is found throughout the Applicants' specification (e.g., page 27, line 4; page 33, line 22; page 42, line 6). Simply stated, McGinty does not teach or suggest the use of a flexible polymer outer shell. In direct contrast, McGinty teaches a "hardened" shell (McGinty, Col. 5, line 20; Col. 8, lines 50-51; Col. 9, line 8; Col. 10, lines 22-23; Col. 15, line 33). Further, while the Examiner properly points out that Applicant is not presently claiming a method of manufacturing microcapsules, it does not follow that a showing of the method of manufacturing of a composition of matter is irrelevant to distinguish that composition. The Applicants are merely using deductive logic to come to a conclusion relative to a composition's characteristic(s). If analyzing McGinty's method can lead one of ordinary skill in the art to conclude that a characteristic does or does not exist, this analysis is relevant and on point. The salient point to be made here is that the process by which McGinty manufactures microcapsules results in a completely different composition of matter from the compositions of the microcapsules of the present invention. To wit, McGinty teaches a multiple step method of making "hardened microspheres": a) forming a water/oil (W/O) emulsion, b) followed by dispersion of that emulsion into another dispersion oil to make an W/O/"O" multiphase emulsion, c) followed by pouring that multiple emulsion over an immiscible solution of PLA or PLGA polymer, dissolved in an immiscible solvent (acetonitrile), d) followed by agitation with a propeller for 24 hours, and later e) reduced pressure evaporation (48 hours) to eliminate the organic solvent residues to form "hardened microspheres" containing the active compound dispersed in "tiny droplets" of the innermost oil phase which is dispersed throughout the internal polymer matrix of the microsphere. McGinty's W/O/"O" emulsion and solvent evaporation phase combination, wherein this combination produces the hardened microsphere, is in every embodiment of his methods (ref: McGinty, Col. 13, lines 21-35). Further, this W/O/"O" emulsion and evaporation phase is in every example supplied by McGinty (ref: McGinty, Example 1 [Col. 15, lines 27-33], Example 2 [Col. 16, line 61; Col. 17, lines 5-6, wherein "W/O" emulsion in acetonitrile is synonymous with W/O/"O" ref: Col. 15, line 28], Example 3 [Col. 18, lines 31-32, Col. 18, line 65], Example 4 [Col. 19, lines 62-63], Example 5 [Col. 21, lines 35-38], Example 6 [Col. 23, lines 55-56], and Example 7 [Col. 29, lines 3-9]). Therefore, by logical

deduction, the Applicants argue that all embodiments of the microspheres taught by McGinty comprise a hardened outer shell, which is in direct contrast to the flexible outer membrane as in all of Applicants independent claims, as amended.

III.B. Multi-Phase and Direct Contact vs. No Direct Contact of Molecular Compounds as well as Dissolved vs. Not Dissolved

Second, the Examiner correctly states that McGinty discloses a multi-phase polymeric microcapsule (ref: 12/28/2004 Office Action, page 6, line 1). Further, the Examiner correctly states that the Applicants claim multi-liquid phases, either as a plurality or one or more liquid phases. However, the Applicants respectfully argue that the Examiner is incorrect relative to the statement that McGinty's multi-phase disclosure anticipates the Applicants' multi-phase disclosure, at least as directed to claims 1, 30-35, 40, and 85-86 (which claim two or more liquid phases). The rationale for this assertion is because the Applicants' multi-phase disclosure is further limited by direct contact between a polymer membrane and one of the liquid phases, which contains certain elements.

The Applicants have further amended "energy absorbing compounds" with "energy absorbing trigger particles" to clarify that the energy absorbing trigger particles are not dissolved in the liquid phase in contact with the outer polymer membrane. Support for this amendment is found in the Applicants' specification, page 62, lines 2-6 (ref: "trigger" and "particulates") as well as page 41, line 24 (ref: "microparticles"). Still further, the Applicants have amended all of the subject independent claims to include direct contact of trigger particles with the outer polymer membrane via sedimentation. Support for this amendment is found in the Applicants' specification, page 62, line 22. Also, the Applicants have amended Claim 1 to specify that the energy absorbing particles are co-encapsulated with the internal, immiscible liquids by the outer polymer membrane. This amendment also clarifies that the particles are not dissolved in the liquids. And finally, the Applicants have amended Claim to include metals in the group of energy absorbing trigger particles. Support for this amendment can be found on page 62, line 11 of the Applicants' specification (ref: "metallic particles").

It is noted that the Examiner referenced Tsuei et al. USPN 5,589,194 (hereinafter referred to as Tsuei) in a previous Office Action. Tsuei teaches filler components including graphite and carbon, which are two of the energy absorbing compounds in the relevant independent claims (ref: Tsuei, Col. 5, lines 35-36). However, Tsuei's filler components are incorporated in his solid matrix-forming material (ref: Tsuei, Col. 5, lines 28-35), which is analogous to the Applicants' outer membrane. Tsuei does not teach the use of graphite and carbon as encapsulated substances, which he defines as "active components." And certainly, Tsuei does not teach the use of graphite or carbon contained in a liquid phase wherein the liquid phase is in direct contact with an outer polymer membrane.

The Examiner correctly advocates that McGinty also discloses, at least some, of the elements claimed by the Applicants (ref: 12/28/2004 Office Action, page 6, lines 13-17), and the Examiner references McGinty's Table 1 found in Col. 15. The Applicants' have amended all of the subject independent claims to strike specific elements that are not necessarily "energy absorbing trigger particles" and respectfully invite the Examiner to re-evaluate these independent claims with respect to McGinty. The removed elements were not energy absorbing compounds per se and the Applicants apologize for the confusion that has resulted.

The Applicants also generally argue that McGinty does not teach the use of particles and certainly not particles in contact with an outer polymer membrane. "Molecular compounds" are defined in Col. 5, lines 57-66 of McGinty. Essentially, molecular compounds are drugs encapsulated by McGinty's microspheres. McGinty specifically states that his "molecular compounds" are not in direct contact with his polymer shell (ref: McGinty, Col. 4, lines 47-50). Therefore, upon closer inspection, the Applicants' advocate that McGinty does not meet the limitations of the Applicants' claims. Further, McGinty does not disclose prior art references that contain both a multi-phase and direct contact of particles with a polymer shell. McGinty's "conventional" disclosure in Col. 4, line 50-53 discloses a single phase of a dissolved drug in contact with a polymer shell, but not a multi-phase wherein particles or non-dissolved elements are in direct contact with a polymer shell. McGinty also discloses multi-walled polymer shells (ref: McGinty, Col. 2, lines 65-66). But, McGinty simply does not disclose a multi-phase application wherein the trigger particles as claimed by the Applicants are in direct contact with a

polymer membrane. As stated above, a rejection under 35 U.S.C. §102 must contain every element recited in the claim in as complete detail as is contained in the claim. In short, McGinty simply does not contain every element in as complete detail as recited in the subject claims.

Therefore, the Applicants traverse the Examiner's rejections and respectfully argue that the reference is not proper under §102 for failure to contain every element recited in the claim in as complete detail as is contained in the claim and arranged as recited in the claim.

IV. Rejections- 35 USC §103

IV.A. Claims 1, 6, 9-23, 26-35, 37-41, 43, 69, 72-78, 83-87, 93-94

The Examiner has rejected claims 1, 6, 9-23, 26-35, 37-41, 43, 69, 72-78, 83-87, 93-94 under 35 U.S.C. 103(a) as being unpatentable over McGinity in view of Grinstaff (USPN 5,665,383, hereinafter referred to as "Grinstaff"). The Applicants respectfully traverse this rejection for the following reasons.

IV.A.1 All Claim Limitations Must Be Considered

The references do not teach or suggest all the claim limitations. When evaluating a claim for determining obviousness, all limitations of the claim must be evaluated. MPEP §2143.03 states:

> To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.

Because from the facts derived from the references, as set forth below, the references do not teach or suggest all of the claim limitations, and thus, the rejection is unsupported by the art and should be withdrawn.

All of Applicants' independent claims have been amended to include a structural limitation of a flexible polymer outer membrane. Simply stated, neither McGinty nor Grinstaff

teach or suggest a flexible polymer outer membrane. A word search of "flexible," "soft," "ductile," and "elastic" in McGinty yielded no results. A word search of "flexible," "ductile," and "elastic" in Grinstaff yielded no results. A word search of "soft" yielded several results in Grinstaff, however, the results were limited to soft tissue.

Therefore, the Applicants traverse the Examiner's rejections and respectfully argue that a *prima facie* case of obviousness has not been established.

IV.A.2 Teaching Away

The references teach away from the Examiner's proposed combination. MPEP §2145 states:

> It is improper to combine references where the references teach away from their combination.

Because from the facts derived from the references, as set forth below, the references teach away from the proposed combination, the rejection is unsupported and should be withdrawn.

The Examiner correctly points out in the 12/28/04 Office Action (ref: beginning on page 8, line 19) that preferred embodiments do not constitute "teaching away." The Applicants apologize for their previous arguments. The Applicants respectfully request a fresh line of arguments.

First, in all of the Applicants' independent claims (i.e., claims 1, 41, 69, 72-78, 83-87), a "direct contact" limitation exists, wherein the outer shell is in direct contact with a liquid phase containing certain listed elements. In sharp contrast, McGinty underscores his teaching that direct contact with his "molecular compounds" must be avoided for his application (ref: McGinty, Col. 2, line 35 through Col. 3, line 46; Col. 12, lines 65-68). It is noted that McGinty is concerned with slow-release applications (ref: McGinty, Col. 1, lines 30; Col. 3, line 28), which is a sharp difference as compared to the Applicants' "burst release" application. Specifically, McGinty states, "*Direct contact* of drug particles with a polymer matrix has been observed *to contribute to degradation of a protein*, ..." (emphasis added) (ref: McGinty, Col. 2, lines 38-40). McGinty also states, "Present techniques used by biotechnology and

pharmaceutical companies to encapsulate peptides...unfortunately suffers from the disadvantage of...*instability due to contact* of the biological agent with the polymer ..." (emphasis added) (ref: McGinty, Col. 3, lines 38-44). The next question for analysis is, "do all embodiments in McGinty lack 'direct contact'?" The quick answer is "yes" for the following reasons. McGinty states, "The present invention provides a unique *multi-phase* microsphere system ..." (emphasis added) (ref: McGinty, Col. 3, lines 63-64). "Multi-phase" is defined as "a modified matrix type microsphere wherein the molecular compound is *not* in direct contact with the polymer ..." (emphasis added) (ref: McGinty, Col. 4, lines 47-49). "Molecular compound" is defined as essentially the load contained in McGinty's microsphere such as drugs, proteins, peptides, and chemicals (ref: McGinty, Abstract; Col. 5, lines 57-66). Thus, upon careful reading, the explicit teaching of McGinty precludes a modification of McGinty's microsphere to include direct contact of his molecular compounds or Grinstaff's biologic agents with an outer polymer shell.

Second, all of Applicants' independent claims have been amended to include the limitation of "flexible" as a structural characteristic of the polymer outer membrane. As stated *supra*, support for this amendment is found throughout the Applicants' specification (e.g., page 27, line 4; page 33, line 22; page 42, line 6). In direct contrast, McGinty teaches a "hardened" microsphere (ref: McGinty, Col. 5, line 20; Col. 8, lines 50-51; Col. 9, line 8; Col. 10, lines 22-23; Col. 15, line 33). McGinty's teaching of a hardened microsphere is logical considering his clear theme and motivation of "slow-release." Does the "hardened" characteristic exist for all embodiments of McGinty? The Applicants argue "yes" and point the reader to Section III.A of this paper for the Applicants' rationale. Further, as stated *supra*, a word search of "flexible," "soft," "ductile," and "elastic" in McGinty yielded no results. Still further, McGinty provides clear motivation for his invention in his "Background of the Art" section contained in Columns 1-3. This motivation aligns itself with the "hardened" characteristics as taught by McGinty. The Applicants argue that "hardened" is a characteristic in all of McGinty's microsphere embodiments. Therefore, upon careful reading, McGinty's explicit teaching precludes a modification of his outer polymer shell from a hardened shell to a flexible membrane.

Third, the invention taught by McGinty requires emulsification (ref: McGinty, Col. 4, line 3) to achieve a hardened outer shell and the invention taught by Grinstaff explicitly avoids

emulsification (ref: Grinstaff, Col. 6, lines 17-20; Col. 7, lines 20-22) to prevent allergic reactions that a resultant microparticle may cause. Thus, if one reference explicitly requires emulsification and the other reference explicitly does not use emulsification and teaches against emulsification (ref: Grinstaff, Col. 2, lines 52-55), there simply cannot be a basis in the references to combine McGinty and Grinstaff. Thus, upon careful reading, McGinty and Grinstaff teach away from the Examiner's proposed combination.

In summary, for the reasons stated above, the combination of McGinty and Grinstaff is not a proper combination for the Examiner's §103 rejection.

IV.A.3 References are not Properly Combinable or Modifiable if the Primary Reference's Intended Function is Destroyed

The combination or modification of the references in the manner suggested by the Examiner would render the primary reference inoperable for its intended purpose. MPEP §2143.01 states:

> If [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.

Because from the facts derived from the references, as set forth below, the suggested combination or modification would render the primary reference inoperable for its intended purpose, the rejection is unsupported by the art and should be withdrawn.

The primary reference (McGinty) describes his "basic technological breakthrough" as "preparing *slow-release*, long-acting, *multi-phase* microspheres" (emphasis added) (ref: McGinty, Col. 5, lines 46-48). As stated supra, slow-release is directly linked to McGinty's hardened outer shell (ref: detailed arguments in Section III.A. of this paper) and multi-phase is directly linked to McGinty's requirement of no direct contact between his molecular compound and outer shell (ref: McGinty, Col. 4, lines 47-50). First, if a flexible membrane is incorporated, this proposed element would destroy McGinty's intended function of slow release or long term therapeutic release. Second, if direct contact between the outer shell and the molecular

compound (i.e., drugs) existed, this proposed limitation would destroy McGinty's intended function.

Therefore, the Applicants traverse the Examiner's rejections and respectfully argue that a *prima facie* case of obviousness has not been established.

IV.A.4 Proposed Modification Cannot Change the Principal of Operation of the Primary Reference

The combination or modification of the references in the manner suggested by the Examiner would change the principle of operation of the primary reference. MPEP §2143.01 states:

> If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.

Because from the facts derived from the references, as set forth below, the suggested combination or modification would change the principle of operation of the primary reference, the rejection is unsupported by the art and should be withdrawn.

As stated explicitly by the primary reference (McGinty), a principle operation of McGinty's invention is for "long term therapeutic release of a biologically active molecule for therapeutically effective periods of time" (ref: McGinty, Abstract, lines 18-20). Combining a flexible outer membrane, as now claimed in all of Applicants' independent claims, with McGinty would change the principal operation of McGinty's microspheres. As stated *supra*, Applicants' motivation for a flexible outer membrane is for burst release of the microcapsule's contents, which is achieved by encapsulation of energy absorbing "trigger" particles.

Therefore, the Applicants traverse the Examiner's rejections and respectfully argue that a *prima facie* case of obviousness has not been established.

IV.B. Claims 26-29, 41, 72, 78, 87--"Magnetic Particles"

The Examiner has rejected claims 26-29, 41, 72, 78, 87 under 35 U.S.C. 103(a) as being unpatentable over McGinity in view of Grinstaff. The subject claims all explicitly claim one or more magnetic particles and a multi-liquid phase wherein one of the liquid phases is in direct contact with the polymer membrane. The Applicants respectfully traverse this rejection for the following reasons in addition to the arguments in Section IV.A of this paper.

The Applicants have amended the relevant independent claims to include the limitation of a "solid" magnetic particle to clarify that the particle is not dissolved in a liquid phase. Further, it is noted that the Examiner referenced Jacob et al. USPN 5,985,312 (hereinafter referred to as Jacob) in a previous Office Action. Jacob teaches metal and magnetic elements (ref: Jacob, Col. 13, lines 46-55). However, Jacob incorporates and integrates his metal/magnetic element in his outer polymer shell to enhance the bioadhesive properties of the polymer shell (ref: Jacob, Col. 3, lines 42-47; Col. 4, lines 37-40; Col. 4, lines 47-56; Col. 13, lines 56-57). Jacob does not teach the encapsulation of magnetic particles in a liquid phase wherein the liquid phase is in contact with an outer polymer membrane.

Before going further, the Applicants respectfully request additional information relative to the Examiner's statement that McGinty teaches magnetic particles (ref: 12/28/2004 Office Action, page 7, paragraph 7, line 16). The Examiner references McGinty, Col. 28, lines 1-50. However, the Applicants are unclear as to where a magnetic particle is taught in this McGinty excerpt. The Examiner argues that since magnetic particles are disclosed in McGinty, motivation for the modification of his invention to include magnetic particles exists. Therefore, it is very important to fully understand which of the elements listed in McGinty, Col. 28, lines 1-50 is/are magnetic particles. An identification of the specific magnetic element(s) is earnestly requested.

IV.B.1. There Must Be a Basis in the Art to Combine/Modify

There must be a basis in the art for combining or modifying the references. MPEP §2143.01 provides:

The mere fact that references can be combined or modified does not render the resultant

combination obvious unless the prior art also suggest the desirability of the combination.

Accordingly, even if all the elements of a claim are disclosed in various prior art references, the claimed invention taken as a whole cannot be said to be obvious without some logical reason given in the prior art why one of ordinary skill would have been prompted to combine the teachings of the references to arrive at the claimed invention. The Applicants submit the following comments and arguments.

First, for the sake or argument, it will be assumed that McGinty does not teach or suggest the use of magnetic particles as argued by the Applicants. Second, it is argued that there is no teaching or suggestion in Grinstaff relative to multi-liquid phases (ref: Grinstaff, FIG. 1). Grinstaff does teach a combination of a liquid-solid phase or specifically, the suspension of solid elements in a liquid (ref: Grinstaff, Col. 12, 33-38). But again, Grinstaff does not teach multi-liquid phases. Third, Grinstaff does teach paramagnetic cations for MRI contrast agents. However, Grinstaff's cations are inherently dissolved and are not solids. And fourth, McGinty does teach a multi-phase microsphere system (ref: McGinty, Col. 3, line 63-64).

So, the question at issue is: "Is there a suggestion or motivation in either McGinty or Grinstaff for combining magnetic particles in a multi-liquid phase?"

First, McGinty will be analyzed. Respectfully, the Applicants point the Examiner to McGinty's multi-phase definition found in Col. 4, lines 47-49. McGinty explicitly teaches a multi-phase wherein a molecular compound is not in direct contact with the polymer shell. Conversely, the Applicants teach a multi-liquid phase wherein one of the liquid phase containing certain elements is in direct contact with a polymer membrane. If McGinty requires no direct contact between his molecular compound and his polymer shell, then clearly there is no motivation in McGinty to modify his invention to include magnetic particles in a liquid phase wherein this liquid phase is in direct contact with a polymer shell. McGinty is concerned about slow-release or long-term therapeutic release of drugs. Given this, McGinty has no motivation for incorporating MRI contrasting agents (as taught by Grinstaff), which require relatively quick release as compared to McGinty's slow-release motivation (weeks or even months at a time [ref: McGinty, Col. 1, lines 36-39]). Simply stated, there is no motivation or suggestion in McGinty

for modifying his invention to include magnetic particles in direct contact with his polymer shell.

Second, Grinstaff will be analyzed. Although Grinstaff does not limit himself to oxygen and contrasting agents for what he calls his "biologics," Grinstaff is clearly motivated by these two specific biologics (ref: Grinstaff, Col. 3, line 8 through Col. 5, line 59). The Applicants respectfully argue that there is no explicit motivation or implicit suggestion in Grinstaff relative to a multi-liquid phase biologic. Again, Grinstaff is primarily motivated by delivering homogeneous oxygen or contrasting agents using a passive delivery means. Therefore, the need for a multi-liquid phase biologic simply does not exist for Grinstaff's motivation and application. Further, Grinstaff does not teach or suggest the use of magnetic particles. Grinstaff teaches paramagnetic cations. Cations are inherently dissolved and not solid.

Therefore, the Applicants traverse the Examiner's rejections and respectfully argue that a *prima facie* case of obviousness has not been established for claims 26-29, 41, 72, 78, 87.

IV.C. Claims 29, 41, 69, 78, 83, 84, 87--"Curie Temperature"

The Examiner has rejected claims 29, 41, 69, 78, 83, 84, 87 under 35 U.S.C. 103(a) as being unpatentable over McGinity in view of Grinstaff. The subject claims all explicitly claim one or more magnetic particles having either a specific Curie temperature or Curie point or effectively a Curie temperature/point higher than the melting temperature of the polymer membrane. The Applicants respectfully traverse this rejection for the following reasons in addition to the arguments presented in Section IV.A of this paper.

IV.C.1 All Claim Limitations Must Be Considered

The references do not teach or suggest all the claim limitations. When evaluating a claim for determining obviousness, all limitations of the claim must be evaluated per MPEP §2143.03 as stated *supra*. Because from the facts derived from the references, as set forth below, the references do not teach or suggest all of the claim limitations, and thus, the rejection is unsupported by the art and should be withdrawn.

Simply stated, McGinty and Grinstaff do not teach or suggest magnetic particles having a Curie temperature/point higher than the melting point of an outer membrane. The significance of this particular limitation can be succinctly found in the Applicants' specification on page 40, lines 7-13. Grinstaff does teach paramagnetic cations. However, "paramagnetic" means the element is at a temperature above its Curie temperature. Therefore, Grinstaff has no motivation for utilizing a Curie temperature higher than the melting point of an outer membrane.

Therefore, the Applicants traverse the Examiner's rejections and respectfully argue that a *prima facie* case of obviousness has not been established.

IV.C.2 There Must Be a Basis in the Art to Combine/Modify

There must be a basis in the art for combining or modifying the references per MPEP §2143.01 as stated *supra*. Accordingly, even if all the elements of a claim are disclosed in various prior art references, the claimed invention taken as a whole cannot be said to be obvious without some logical reason given in the prior art why one of ordinary skill would have been prompted to combine the teachings of the references to arrive at the claimed invention. The Applicants submit the following comments and arguments.

The Examiner did provide references but did not particularly point out a motivation or suggestion, either explicitly or implied, in either of the references. Based on the fact that the Examiner did not particularly point out a motivation or suggestion, either explicitly or implied, it is interpreted that the Examiner is basing the proposed combination on "common knowledge" or "common sense." MPEP §2144.03.A as recently amended states:

> It would not be appropriate for the examiner to take official notice of facts without citing a prior art reference where the facts asserted to be well known are not capable of *instant and unquestionable* demonstration as being well-known. For example, assertions of technical facts in the areas of esoteric technology or specific knowledge of the prior art must always be supported by citation in the pertinent art. (emphasis added)

The standard of "instant and unquestionable" demonstration of being well-known is undeniably a high standard. The Applicants respectfully challenges that the Examiner's rejection is not

properly officially noticed and not properly based upon common knowledge for the following reasons.

First, the Applicants incorporation of magnetic particles in the subject claims is based on their motivation to use the magnetic particles as trigger agents to melt at least a portion of their outer polymer membrane and release the liquid contents of their microcapsule (ref: Applicants' specification, page 40, lines 7-13). Therefore, the subject limitation is grounded in medical and technical design. The Examiner is required by MPEP §2144.03.A to provide technical facts or specific knowledge in prior art references relative to the relationship of a Curie temperature magnetic particles and a melting temperature of a outer polymer membrane.

Second, it is important to note that both McGinty and Grinstaff rely on passive release of their encapsulated contents. Therefore, McGinty and Grinstaff have no motivation associated with a relative difference between a Curie temperature of a magnetic particle and a melting temperature of an outer polymer membrane. Thus, neither McGinty nor Grinstaff contain the technical facts or specific knowledge required by MPEP §2144.03.A.

Therefore, the Applicants traverse the Examiner's "common knowledge" rejections, respectfully argue that a *prima facie* case of obviousness has not been established under the current law, and respectfully demand that the Examiner produce proper authority the rejection as it relates to claims 29, 41, 69, 78, 83, 84, 87.

IV.D. Claim 27--"Ceramic Coating"

The Examiner has rejected claim 27 under 35 U.S.C. 103(a) as being unpatentable over McGinity in view of Grinstaff. The subject claim includes a ceramic coating. The Applicants respectfully traverse this rejection for the following reasons in addition to the arguments presented in Section IV.A of this paper.

The references do not teach or suggest all the claim limitations. When evaluating a claim for determining obviousness, all limitations of the claim must be evaluated per MPEP §2143.03 as stated *supra*. Because from the facts derived from the references, as set forth below, the references do not teach or suggest all of the claim limitations, and thus, the rejection is

unsupported by the art and should be withdrawn.

Simply stated, McGinty and Grinstaff do not teach or suggest a ceramic coating around magnetic particles. The Examiner curiously equates PVP with a ceramic (ref: 12/28/2004 Office Action, page 8, lines 7-8). It is commonly known in the art that Polyvinylpyrrolidone (PVP) is a macromolecular polymer of N-vinylpyrrolidone and not a ceramic. A word search of "ceramic" in both McGinty and Grinstaff yielded no results.

Further, There must be a basis in the art for combining or modifying the references. MPEP §2143.01 provides:

> The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggest the desirability of the combination.

Accordingly, even if all the elements of a claim are disclosed in various prior art references, the claimed invention taken as a whole cannot be said to be obvious without some logical reason given in the prior art why one of ordinary skill would have been prompted to combine the teachings of the references to arrive at the claimed invention.

Again, simply stated, McGinty and Grinstaff do not provide a suggestion or motivation for combining/modifying their invention to include a ceramic coating to surround a magnetic particle.

Therefore, the Applicants traverse the Examiner's rejections and respectfully argue that a *prima facie* case of obviousness has not been established.

IV.E. Claim 29--"Specific Curie Temperature Range"

The Examiner has rejected claim 29 under 35 U.S.C. 103(a) as being unpatentable over McGinity in view of Grinstaff. The subject claim includes a limitation of a Curie temperature from about 41 degrees C to about 95 degrees C. The Applicants respectfully traverse this rejection for the following reasons in addition to the arguments presented in Section IV.A of this paper.

The references do not teach or suggest all the claim limitations. When evaluating a claim

for determining obviousness, all limitations of the claim must be evaluated per MPEP §2143.03 as stated *supra*. Because from the facts derived from the references, as set forth below, the references do not teach or suggest all of the claim limitations, and thus, the rejection is unsupported by the art and should be withdrawn.

Simply stated, McGinty and Grinstaff do not teach or suggest a magnetic particle having a Curie temperature from about 41 degrees C to about 95 degrees C (or equivalently from about 105.8 degrees F to about 203 degrees F).

The Applicants respectfully traverse the rejection as it relates to amended claim 29 and argue that the Examiner has not established a *prima facie* case of obviousness.

IV.F. Claims 41, 69, 72, 78, 83, 84, 87--"Coating Added as a Limitation"

The Examiner has rejected claims 41, 69, 72, 78, 83, 84, and 87 under 35 U.S.C. 103(a) as being unpatentable over McGinity in view of Grinstaff. It is noted that Tsuei teaches the encapsulation of magnetic oxides for steering particles for drug delivery (ref: Tsuei, Col. 4, lines 24-25). The subject claims have been amended to include the following limitation: a coating surrounding at least one of the one or more magnetic particles, the coating selected from the group consisting of ceramics, metacrylates, alginates, dextran, polyacrylates, and polyvinyl pyrrolidine. Support for this amendment is found in the Applicants specification on page 8, line 23 through page 9, line 7. The Applicants respectfully traverse this rejection for the following reasons in addition to the arguments presented in Section IV.A of this paper.

The references do not teach or suggest all the claim limitations. When evaluating a claim for determining obviousness, all limitations of the claim must be evaluated per MPEP §2143.03 as stated *supra*. Because from the facts derived from the references, as set forth below, the references do not teach or suggest all of the claim limitations, and thus, the rejection is unsupported by the art and should be withdrawn.

Simply stated, McGinty and Grinstaff (as well as Tsuei) do not teach or suggest a coating surrounding magnetic particles. Grinstaff teaches the use of paramagnetic cations, not magnetic particles, for MRI contrasting agents (ref: Grinstaff, Col. 5, lines 33-37). Grinstaff does teach

the use of PVP (ref: Grinstaff, Col. 28, line 16). However, Grinstaff does not teach or suggest a coating to surround his paramagnetic cations. And Grinstaff does not teach or suggest the use of PVP as a coating to surround a magnetic particle. As stated *supra*, Tsuei teaches the encapsulation of magnetic oxides, but does not teach or suggest a coating to surround his magnetic oxides.

Further, there must be a basis in the art for combining or modifying the reference per MPEP §2143.01 as discussed *supra*. Accordingly, even if all the elements of a claim are disclosed in various prior art references, the claimed invention taken as a whole cannot be said to be obvious without some logical reason given in the prior art why one of ordinary skill would have been prompted to combine the teachings of the references to arrive at the claimed invention.

Of the references, as stated above, Grinstaff teaches the use of paramagnetic cations. However, Grinstaff does not provide a suggestion or motivation for coating his paramagnetic cations. Simply stated, there is no motivation to coat the parmagnetic cations of Grinstaff or the magnetic oxides of Tsuei.

The Applicants respectfully traverse the rejection as it relates to amended claim 41 and argue that the Examiner has not established a *prima facie* case of obviousness.

The "obviousness" basis for rejection of the claims being obviated in view of the remarks above, Applicants respectfully request removal of this basis for rejection. In particular, claims 6, 10,12-13, 15-16, 18-20, 39, 41, 43, 69, 72, 76-84, 87, and 93-94 have been amended to overcome the "new matter" rejection, and are not further rejected under 102(b) or other basis. Therefore, at least these claims appear to be allowable in view of Applicants' arguments and such allowance is requested.

V. Claim Objections

Claims 24-25 were objected to by the Examiner as being dependent upon a rejected base claim. Applicants assume that Examiner makes this basis of rejection over and above the

rejection of the other claims such that if claims 24-25 were amended to recite all limitations of the claims from which they depend, they would be allowable. To this end, new claims 95 and 96 are added here to address the Examiner's intent. These claims should be allowable and such allowance is requested.

VI. Conclusion

This response constitutes a complete response to all issues raised in the Office Action mailed December 28, 2004. In view of the remarks and amendments to the claims traversing rejections presented therein, Applicants assert that pending claims 1, 6, 9-35, 37-41, 43, 69, 72-78, 83-87, 93-94 are in condition for allowance. Applicant's representative listed below respectfully requests the courtesy of a phone call from the Examiner to discuss the case, these remarks and amendments, and the finality of the rejections.

NASA Johnson Space Center hereby authorizes the Commissioner to charge any fees necessary to NASA Johnson Space Center Deposit Account No. 14-0116 for the filing of these documents.

Respectfully submitted,

Date: 6/28/05

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